

Fig. 1

CAAGGAGATGGCGCCCAACAGTCCCCCGGCCACGGGGCCTGCCACCATACCCACGCCGAAACAAGCGCTC  
 ATGAGCCCGAAGTGGCGAGCCCGATCTTCCCATCGGTGATGTCGGCGATATAGGCGCCAGCAACCGCAC  
 CTGTGGCGCGCGGTGATCCCGGCCAGGATGCGTCCGGCTAGAGGATCGAGATCTCGATCCCGCGAAATTA  
 ATACGACTCACTATAGGGGAATTGTGAGCGGATAACAATTCCCCTCTAGAAATAATTTTGTTTAACTTTA  
 AGAAGGAGATATACATATGGGCGCCGGCACCCCGGTGACCGCCCCGCTGGCGGGCACTATCTGGAAGGTG  
 CTGGCCAGCGAAGGCCAGACGGTGGCCGAGGCGAGGTGCTGCTGATTCTGGAAGCCATGAAGATGGAAA  
 CCGAAATCCGCGCCCGCGAGGCCGGGACCGTGCGCGGTATCGCGGTGAAAGCCGGCGACGCGGTGGCGGT  
 CGGCGACACCCGTGATGACCCGTGGCGGGCTCTGGATCCGATCTGTACGACGATGACGATAAGGGAATTATC  
 ACAAGTTTGTACAAAAAGCTGAACGAGAAAACGTAAATGATATAAATATCAATATATTAAATTAGATTT  
 TGCATAAAAAACAGACTACATAATACTGTAAAAACACAACATATCCAGTCACTATGGCGGCCGATTAGGC  
 ACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATAATGTGTGGATTTTGAGTTAGGATCCGGCGAGAT  
 TTTTCAGGAGCTAAGGAAGCTAAAATGGAGAAAAAAATCACTGGATATACCACCGTTGATATATCCCAATG  
 GCATCGTAAAGAACATTTTGTAGGCATTTTCAGTCAGTTGCTCAATGTACCTATAACCAGACCGTTTCAGCTG  
 GATATTACGGCCTTTTAAAGACCGTAAAGAAAAATAAGCACAAAGTTTTATCCGGCCTTTATTCACATTC  
 TTGCCCCGCTGATGAATGCTCATCCGGAATTCGTATGGCAATGAAAGACGGTGAGCTGGTGATATGGGA  
 TAGTGTTACCCCTTGTTACACCGTTTTCATGAGCAAACTGAAACGTTTTTCATCGCTCTGGAGTGAATAC  
 CACGACGATTTCCGGCAGTTTCTACACATATATTCGCAAGATGTGGCGTGTTACGGTGAAAACCTGGCCT  
 ATTTCCCTAAAGGGTTTATTGAGAATATGTTTTTCGTCTCAGCCAATCCCTGGGTGAGTTTCACCAGTTT  
 TGATTTAAACGTGGCCAATATGGACAACCTCTTCGCCCCCGTTTTTCACCATGGGCAAATATTATACGCAA  
 GGCGACAAGGTGCTGATGCGGATTGCGGATTCAGTTTCATCATGCCGTCTGTGATGGCTTCCATGTCGCA  
 GAATGCTTAATGAATTACAACAGTACTGCGATGAGTGGCAGGGCGGGGCGTAAACGCGTGGATCCGGCTT  
 ACTAAAAGCCAGATAACAGTATGCGTATTTGCGCGCACCGGTGCTAGCGTATACCCGAAGTATGTCAAAA  
 AGAGGTGTGCTATGAAGCAGCGTATTACAGTGACAGTTGACAGCGACAGCTATCAGTTGCTCAAGGCATA  
 TATGATGTCAATATCTCCGCTCTGGTAAGCACAAACCATGCAGAATGAAGCCCGTCTGCTGCGTGCCGAAC  
 GCTGGAAGCGGAAAAATCAGGAAGGGATGGCTGAGGTGCGCCCGTTTTATTGAAATGAACGGCTCTTTTGC  
 TGACGAGAACAGGGACTGGTGAAATGCAGTTTAAAGGTTTACACCTATAAAAGAGAGAGCCGTTATCGTCT  
 GTTTGTGGATGTACAGAGTATATTATTGACACGCCCGGGCGACGGATGGTGATCCCCCTGGCCAGTGCA  
 CGTCTGCTGTGAGATAAAGTCTCCCGTGAACCTTTACCCGGTGGTGCATATCGGGGATGAAAGCTGGCGCA  
 TGATGACCACCGATATGGCCAGTGTCGGGTCTCCGTTATCGGGGAAGAAGTGGCTGATCTCAGCCACCG  
 CGAAAATGACATCAAAAACGCCATTAACCTGATGTTCTGGGGAATATAAATGTCAGGCTCCGTTATACAC  
 AGCCAGTCTGCAGGTGACCATAGTGACTGGATATGTTGTGTTTTACAGTATTATGTAGTCTGTTTTTTA  
 TGCAAAATCTAATTTAATATATTGATATTTATATCATTTTACGTTTCTCGTTCAGCTTTCTTGTACAAAG  
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 TGCCACCGCTGAGCAATAACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTG  
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 AGCATCCAGGGTGACGGTGCCGAGGATGACGATGAGCGCATTTGTTAGATTTTCATACACGGTGCCCTGACTG  
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 GAATTAATTCCTGAAGACGAAAGGCCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAAT  
 GGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTTATTTTTCTAA  
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 GAACTGGATCTCAACAGCGGTAAAGATCCTTGAGAGTTTTTCGCCCCGAAGAAGCTTTTCCAATGATGAGCA  
 CTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTGTGACGCCGGGCAAGAGCAACTCGGTGCGCG  
 CATACTACTTCTCAGAAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATG  
 ACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAA  
 CGATCGGAGGACCGAAGGAGCTAACCCTTTTTTGCACAACATGGGGGATCATGTAACCTCGCCCTTGATCG  
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 ACAACGTTGCGCAAACTATTAACCTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGA  
 TGGAGGCGGATAAAGTTGACAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAA

Fig. 2A

ATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGT  
 ATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAG  
 GTGCCCTCACTGATTAAGCATTGGTAACGTGCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAA  
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 CGTGAGTTTTCTGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTT  
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 GGATAAGGCGCAGCGGTGCGGGCTGAACGGGGGGTTCGTGCACACAGCCAGCTTGGAGCGAACGACCTAC  
 ACCGAAGTGAATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACA  
 GGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCAGGAGGCTTCCAGGGGGAAACGCCTGGTA  
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 CGCTCGCCGCGAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCTGATGCGG  
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 ACCCGCAACACCCGCTGACGCGCCCTGACGGGCTTGCTGCTCGCCGCTACCGGCTTACAGACAAGCTGT  
 GACCGTCTCCGGGAGCTGCATGTGTACAGGTTTTCACCGTCATACCGAAACGCGCGAGGCAGCTGCGG  
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 GGTCACTGATGCCTCCGTGTAAGGGGATTTCTGTTTCATGGGGGTAATGATACCGATGAAACGAGAGAGG  
 ATGCTCACGATACGGGTTACTGATGATGAACATGCCCGGTTACTGGAACGTTGTGAGGGTAAACAACCTGG  
 CGGTATGGATGCGGCGGGACCAGAGAAAAATCACTCAGGGTCAATGCCAGCGCTTCGTTAATACAGATGT  
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 TTTTGCAGCAGCAGTCGCTTACGTTGCTCGCTATCGGTGATTGATTCTGCTAACCAGTAAGGCAACC  
 CCGCCAGCCTAGCCGGGTCTCAACGACAGGAGCAGCATCATGCGCACCCGTGGCCAGGACCCAACGCTG  
 CCCGAGATGCGCCGCGTGCGGGCTGCTGGAGATGGCGGACGCGATGGATATGTTCTGCCAAGGGTTGGTTT  
 GCGCATTCACAGTTCTCCGCAAGAATTGATTGGCTCCAATTCTTGGAGTGGTGAATCCGTTAGCGAGGTG  
 CCGCCGGCTTCCATTACAGGTGAGGTGCGCCCGCTCCATGCACCGCGACGCAACGCGGGGAGGCAGACAA  
 GGTATAGGGCGGCGCCTACAATCCATGCCAACCCGTTCCATGTGCTCGCCGAGGCGGCATAAATCGCCGT  
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 GCGAGGGCGTGCAAGATTCCGAATACCGCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGT  
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 AAGTGCGGCGACGATAGTCATGCCCCGCGCCACCGGAAGGAGCTGACTGGGTGAAGGCTCTCAAGGGC  
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 TCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTGCG  
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 GCCCTGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTGGCCAGCAGGCGAAAATCCTGTTTGATGGTG  
 GTTAACGGCGGGATATAACATGAGCTGTCTCGGTATCGTCGTATCCCACTACCGAGATATCCGCACCAA  
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 AGTGGGAACGATGCCCTCATTACGATTTGCGATGGTTTGTGAAAACCGGACATGGCACTCCAGTCGCCT  
 TCCCGTTCCGCTATCGGCTGAATTTGATTGCGAGTGAGATATTTATGCCAGCCAGCCAGACGCGAGCGG  
 CCGAGACAGAACTTAATGGGCCGCTAACAGCGCGATTTGCTGGTGACCAATGCGACCAGATGCTCCAC  
 GCCCAGTCGCGTACCGTCTTCATGGGAGAAAATAATACTGTTGATGGGTGTCTGGTCAGAGACATCAAGA

Fig. 2B

AATAACGCCGGAACATTAGTGCAGGCAGCTTCCACAGCAATGGCATCCTGGTCATCCAGCGGATAGTTAA  
TGATCAGCCCACTGACGCGTTGCGCGAGAAGATTGTGCACCGCCGCTTTACAGGCTTCGACGCCGCTTCG  
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GACGGCGCGTGCAGGGCCAGACTGGAGGTGGCAACGCCAATCAGCAACGACTGTTTGCCCGCCAGTTGTT  
GTGCCACGCGGTTGGGAATGTAATTCAGCTCCGCCATCGCCGCTTCCACTTTTTCCCGCGTTTTTCGCAGA  
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TATAACGTTACTGGTTTCACATTCACCACCCTGAATTGACTCTCTTCCGGGCGCTATCATGCCATACCGC  
GAAAGGTTTTGCGCCATTTCGATGGTGTCCGGGATCTCGACGCTCTCCCTTATGCGACTCCTGCATTAGGA  
AGCAGCCCAGTAGTAGGTTGAGGCCGTTGAGCACCGCCGCCGCAAGGAATGGTGCATG

Fig. 2C

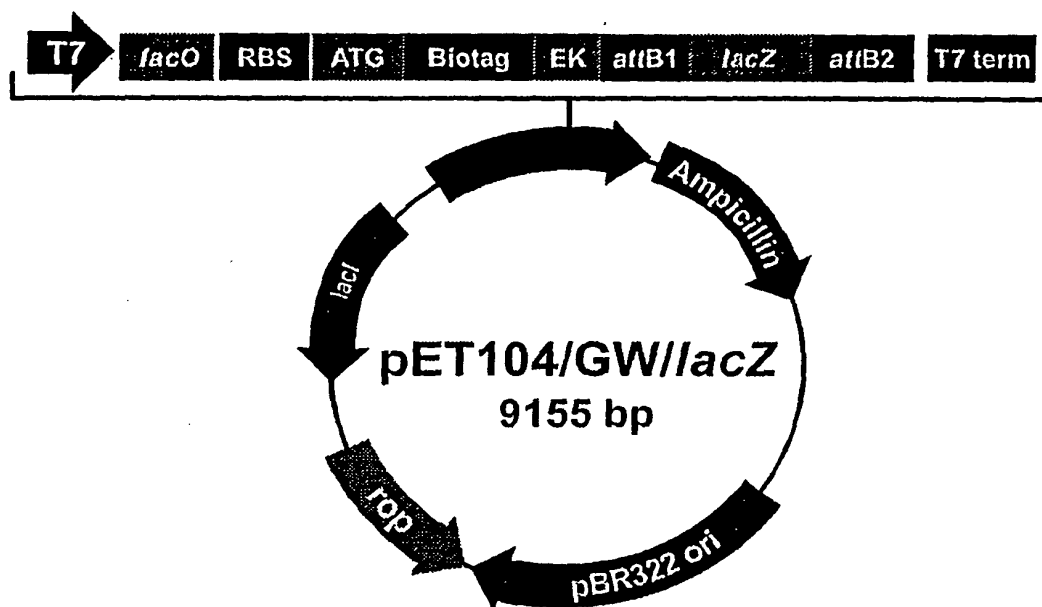


Fig.3

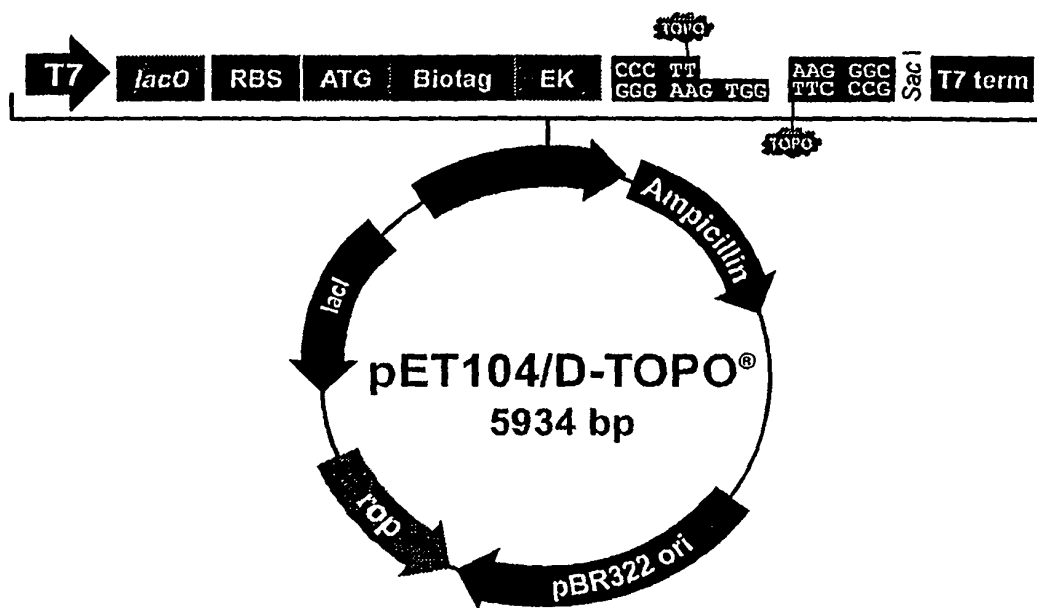


Fig. 4

CAAGGAGATGGCGCCCAACAGTCCCCCGGCCACGGGGCCTGCCACCATACCCACGCCGAAACAAGCGCTC  
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 CTGTGGCGCCGGTGTATGCCGGCCACGATGCGTCCGGCGTAGAGGATCGAGATCTCGATCCCGCGAAATTA  
 ATACGACTCACTATAGGGGAATTGTGAGCGGATAACAATTCCCCTCTAGAAATAATTTGTTTAACTTTA  
 AGAAGGAGATATACATATGGGCGCCGGCACCCCGGTGACCGCCCCGCTGGCGGGCACTATCTGGAAGGTG  
 CTGGCCAGCGAAGGCCAGACGGTGGCCCGAGGCGAGGTGCTGCTGATTCTGGAAGCCATGAAGATGGAAA  
 CCGAAATCCGCGCCGCGCAGGCCGGGACCGTGC CGCGGTATCGCGGTGAAAGCCGGCGACGCGGTGGCGGT  
 CGGCGACACCCTGATGACCCTGGCGGGCTCTGGATCCGATCTGTACGACGATGACGATAAGGGAATTGAT  
 CCCTTCACCAAGGGCGAGCTCAGATCCGGCTGCTAACAAGCCCCGAAAGGAAGCTGAGTTGGCTGCTGCC  
 ACCGCTGAGCAATAACTAGCATAAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAG  
 GAGGAATATATCCGGATATCCCGCAAGAGGCCCGGCAGTACCGGCATAACCAAGCCTATGCCTACAGCA  
 TCCAGGGTGACGGTGGCGAGGATGACGATGAGCGCATTGTTAGATTTTATACACGGTGCCTGACTGCGTT  
 AGCAATTTAACTGTGATAAACTACCGCATTAAAGCTAGCTTATCGATGATAAGCTGTCAAACATGAGAAT  
 TAATTCCTGAAGACGAAAGGCCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTT  
 TCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTATTTTTCTAAATAC  
 ATTCAAATATGTATCCGCTCATGAGACAATAACCCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAG  
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 GGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCG  
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 CTCACTGATTAAGCATTGGTAACGTGTGAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAACTT  
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 TCACGATACGGGTTACTGATGATGAACATGCCCGGTTACTGGAACGTTGTGAGGGTAAACAACCTGGCGGT

Fig. 5A

ATGGATGCGGCGGGACCAGAGAAAAATCACTCAGGGTCAATGCCAGCGCTTCGTTAATACAGATGTAGGT  
GTTCCACAGGGTAGCCAGCAGCATCCTGCGATGCAGATCCGGAACATAATGGTGCAGGGCGCTGACTTCC  
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CAGCCTAGCCGGGTCTCAACGACAGGAGCAGATCATGCGCACCCGTGGCCAGGACCCAACGCTGCCCG  
AGATGCGCCGCGTGGGCTGCTGGAGATGGCGGACGCGATGGATATGTTCTGCCAAGGGTTGGTTTGCGC  
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CGGCTTCCATTACAGGTGAGGTGGCCCGGCTCCATGCACCGCGACGCAACGCGGGGAGGCAGACAAGGTA  
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GGGCGTGCAAGATTCCGAATACCGCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGTCTCTC  
GCCGAAATGACCCAGAGCGCTGCCGGCACCTGTCTACGAGTTGCATGATAAAGAAGACAGTCATAAGT  
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GTCGGGAAACCTGTGTCGAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATT  
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TGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTTGCCCCAGCAGGCGAAAATCCTGTTTGATGGTGGTTA  
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ACGCCGGAACATTAGTGAGGCGAGCTTCCACAGCAATGGCATCCTGGTCATCCAGCGGATAGTTAATGAT  
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GGTTTTGCGCCATTGATGGTGTCCGGGATCTCGACGCTCTCCCTTATGCGACTCCTGCATTAGGAAGCA  
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Fig. 5B



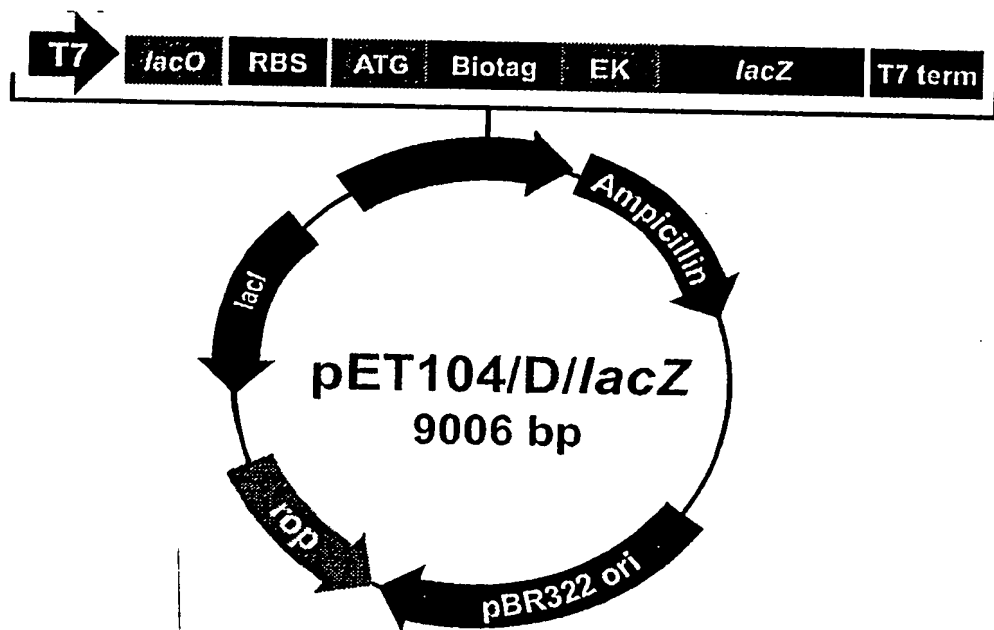


Fig.6

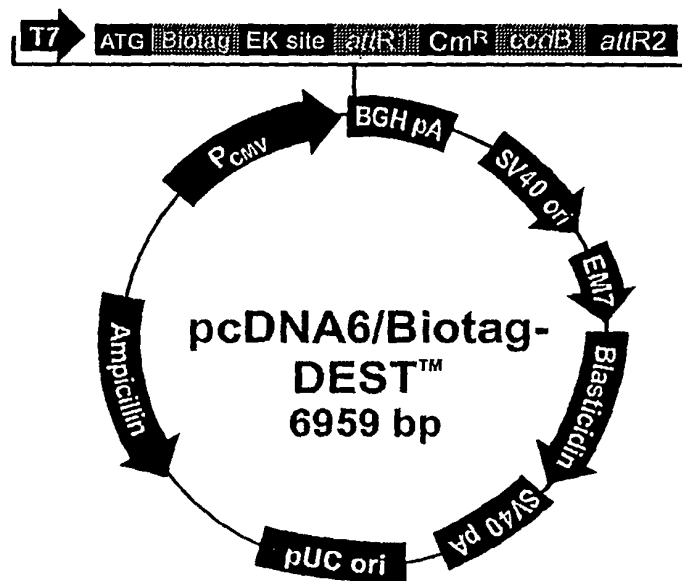


Fig.7

GACGGATCGGGAGATCTCCCGATCCCCTATGGTCTGACTCTCAGTACAATCTGCTCTGATGCCGCATAGTT  
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 CTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGCTAGCGTTTAAACTT  
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 AGGTGCTGATGCCGCTGGCGATTACAGGTTTATCATGCGCTCTGTGATGGCTTCCATGTCGGCAGAATGCT  
 TAATGAATTACAACAGTACTGCGATGAGTGGCAGGGCGGGGCGTAAACGCGTGGATCCGGCTTACTAAAA  
 GCCAGATAACAGTATGCGTATTTGCGCGCTCGCGAACCGGTGTATACCCGAAGTATGTCAAAAAGAGGTG  
 TGCTATGAAGCAGCGTATTACAGTGACAGTTGACAGCGACAGCTATCAGTTGCTCAAGGCATATATGATG  
 TCAATATCTCCGGTCTGGTAAGCACAACCATGAGCAATGAAGCCCGTCTGCTGCGTGCCGAACGCTGGAA  
 AGCGGAAAAATCAGGAAGGGATGGCTGAGGTGCGCCGGTTTTATTGAAATGAACGGCTCTTTTGCTGACGAG  
 AACAGGGACTGGTGAATGCAGTTTAAAGGTTTACACCTATAAAAGAGAGAGCCGTTATCGTCTGTTTGTG  
 GATGTACAGAGTGATATTATTGACACGCCCCGGGCGACGGATGGTGATCCCCCTGGCCAGTGACAGTCTGC  
 TGTCAGATAAAGTCTCCCGTGAACCTTACCCGGTGGTGATATCGGGGATGAAAGCTGGCGCATGATGAC  
 CACCGATATGGCCAGTGTGCCGGTCTCCGTTATCGGGGAAGAAGTGGCTGATCTCAGCCACCGCGAAAAAT  
 GACATCAAAAACGCCATTAACCTGATGTTCTGGGGAATATAAATGTGAGGCTCCGTTATACACAGCCAGT  
 CTGCAGGTCGACCATAGTGACTGGATATGTTGTGTTTTACAGTATTATGTAGTCTGTTTTTATGCAAAA  
 TCTAATTTAATATATTGATATTTATATCATTTTTACGTTTCTCGTTTACGCTTTCTTGTAACAAAGTGGTGAT  
 AATTAATTAAGATCTAGAGGGCCCGTTTAAACCCGCTGATCAGCCTCGACTGTGCCCTTCTAGTTGCCAGC  
 CATCTGTTGTTTGGCCCTCCCCCGTGCTTCTTACCCCTGGAAGGTGCCACTCCCACTGTCTTTCTCTA  
 ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCTATTCTATTCTGGGGGTGGGGTGGGGCAG  
 GACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTG  
 AGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGC  
 GGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTTCGCTTTC  
 TTCCCTTCTTTCTCGCCACGTTTCGCGGCTTTCCCCGTCAAGCTCTAAATCGGGGCATCCCTTTAGGGT  
 TCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCC  
 ATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCT

Fig. 8A

CAAACTGGAACAACACTCAACCCCTATCTCGGTCTATTCTTTTGATTATAAGGGATTTTGGGGATTTTCGG  
 CCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTAACGCGAATTAATTCTGTGGAATGTGTGTCAG  
 TTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGGCAGGCAGAAAGTATGCAAAGCATGCATCTCAATTAGTCA  
 GCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAAGTATGCAAAGCATGCATCTCAATTAGT  
 CAGCAACCATAGTCCCGCCCCCTAACTCCGCCCCATCCCGCCCCCTAACTCCGCCCCAGTCCGCCCCATTCTCC  
 GCCCCATGGCTGACTAATTTTTTTTTTATTATGACAGAGGCCGAGGCCGCCTCTGCCTCTGAGCTATTCCAG  
 AAGTAGTGAGGAGGCTTTTTTGGAGGCCCTAGGCTTTTGCAAAAAGCTCCCGGGAGCTTGTATATCCATTT  
 TCGGATCTGATCAGCACGTGTTGACAATTAATCATCGGCATAGTATATCGGCATAGTATAATACGACAAG  
 GTGAGGAACATAACCATGGCCAAGCCTTTGTCTCAAGAAGAATCCACCCTCATTGAAAGAGCAACGGCTA  
 CAATCAACAGCATCCCCATCTCTGAAGACTACAGCGTCGCCAGCGCAGCTCTCTCTAGCGACGGCCGCAT  
 CTTCACTGGTGTCAATGTATATCATTTTACTGGGGGACCTTGTGCAGAACTCGTGGTGTGGGCACTGCT  
 GCTGCTCGGGCAGCTGGCAACCTGACTTGTATCGTCCGCGATCGGAAATGAGAACAGGGGCATCTTGAGCC  
 CCTGCGGACGGTGCCGACAGGTGCTTCTCGATCTGCATCCTGGGATCAAAGCCATAGTGAAGGACAGTGA  
 TGGACAGCCGACGGCAGTTGGGATTCTGTAATTGCTGCCCTCTGGTTATGTGTGGGAGGGCTAAGCACTT  
 CGTGGCCGAGGAGCAGGACTGACACGTGCTACGAGATTTGCGATTCCACCGCCGCCTTCTATGAAAGGTTG  
 GGCTTCGGAATCGTTTTCCGGGACGCGCGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCT  
 TCGCCACCCCAACTTGTTTTATTGCGACTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTTAC  
 AAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATGTC  
 TGTATACCGTGCAGCTTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCTGTGTGAAATTGTT  
 ATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGT  
 GAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCAGTCGGGAAACCTGTCGTGCCAGCTG  
 CATTAATGAATCGGCCAACGCGCGGGGAGAGGCGTTTGGCGATTGGGCGCTCTTCCGCTTCTCGCTCA  
 CTGACTCGCTGCGCTCGGTCTCGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTT  
 ATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAGGCCAGGAACCGT  
 AAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCT  
 CAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACAGGCGTTTCCCCCTGGAAGCTCCCTCGT  
 CCGCTCTCCTGTTCCGACCCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGCG  
 CTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCTGCTCCAGCTGGGCTGTGTGC  
 ACGAACCCCCCGTTTACGCCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAG  
 ACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCT  
 ACAGAGTTCTTGAAGTGGTGCCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGC  
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 TGGTTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTT  
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 GGATCTTCACCTAGATCCCTTTAAATTAATAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAAC  
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 CAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGC  
 CGAGCGCAGAAGTGGTCTTCAACTTTATCCGCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGA  
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 CGTCGTTTGGTATGGCTTCATTGAGTCCGGTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTT  
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 CTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCTATGCCATCCGTAAGATGCTTTTCTGTGACTG  
 GTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAAT  
 ACGGGATAATACCGCGCCACATAGCAGAACCTTTAAAAGTGCTCATCATTGGAACCGTTCTTCCGGGCGA  
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 CAGCATCTTTTACTTTTACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGGG  
 AATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCTTTTTCAATATTATGAAGCATTATCAG  
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 CATTTCCCGGAAAAGTGCCACCTGACGTC

Fig. 8B

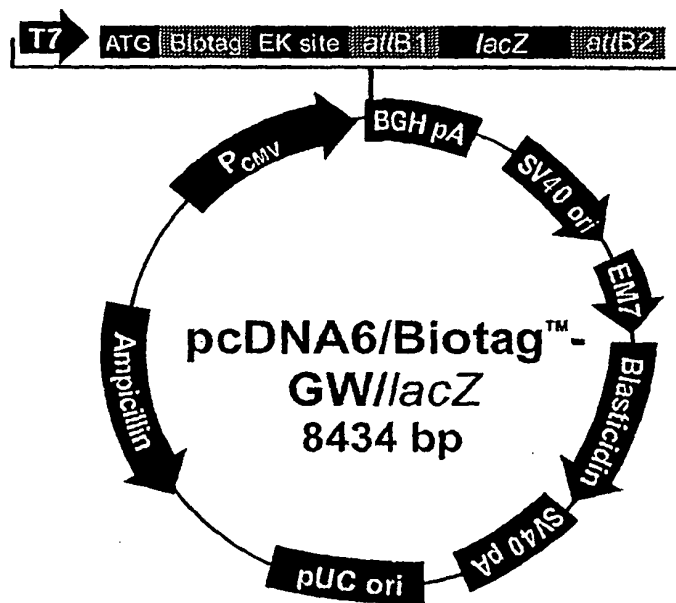


Fig. 9

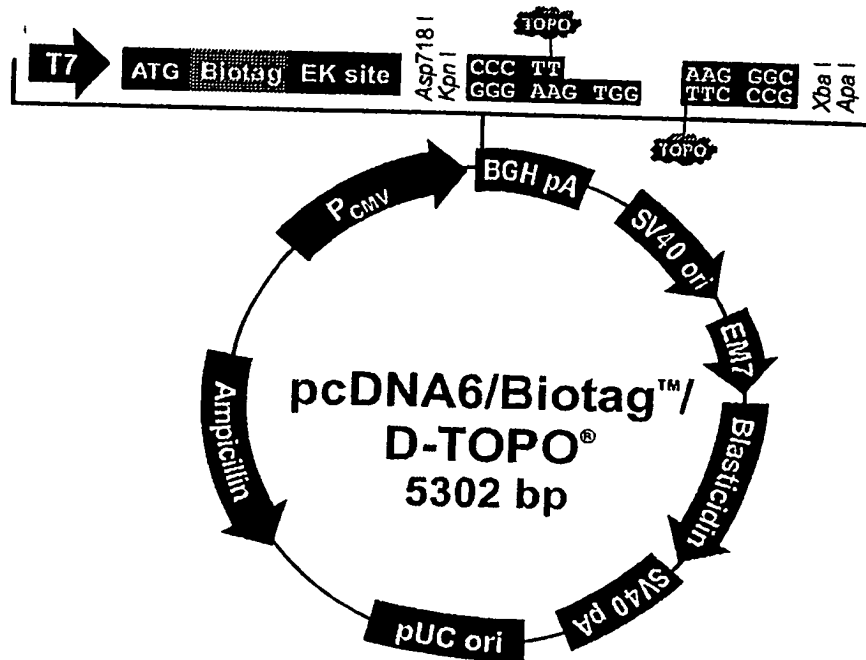


Fig. 10

GACGGATCGGGAGATCTCCCGATCCCCTATGGTCGACTCTCAGTACAATCTGCTCTGATGCCGCATAGTT  
AAGCCAGTATCTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAAATTTAAGCTACA  
ACAAGGCAAGGCTTGACCGACAATTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCG  
ATGTACGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTTC  
ATTAGTTCATAGCCCATATATGGAGTTCGCGCTTACATAAATTACGGTAAATGGCCCGCTGGCTGACCG  
CCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCC  
ATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCC  
AAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCTGGCATTATGCCAGTACATGACCTTA  
TGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC  
AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAA  
TGGGAGTTTGTGTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACCTCCGCCCATTTGACG  
CAAATGGGCGGTAGGCGGTGACGGTGGGAGGTTATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCA  
CTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAGGGAGACCCAAGCTGGCTAGCGTTTTAACTT  
AAGCTTACCATGGGCGCCGGCACCCCGGTGACCGCCCCGCTGGCGGGCACTATCTGGAAGGTGCTGGCCA  
GCGAAGGCCAGACGGTGGCCGCGAGGCGAGGTGCTGCTGATTCTGGAAGCCATGAAGATGGAACCGAAAT  
CCGCGCCGCGCAGGCCGGGACCGTGCGCGGTATCGCGGTGAAAGCCGGCGACGCGGTGGCGGTGGCGGAC  
ACCTGATGACCTGGCGGGCTCTGGATCCGATCTGTACGACGATGACGATAAGGTACCTAGGATCCAGT  
GTGGTGGAAATTGATCCCTTACCAAGGGCGTCGAGTCTAGAGGGCCCGTTTTAAACCCGCTGATCAGCCTC  
GACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGGCCCTCCCCCGTGCTTCTTGAACCTGGAAGGT  
GCCACTCCCCTGCTCCTTTCTTAATAAAATGAGGAAATGAGCAATGCTGCTGAGTAGGTGTCATTCTA  
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TGTAGCGGCGCATTAAGCGCGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCC  
TAGCGCCGCTCCTTTGCTTTCTTCCCTTCTTCTCGCCACGTTGCGCGGCTTTCCCGCTCAAGCTCT  
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GGTGATGGTTACGTAAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGT  
TCTTTAATAGTGGACTCTGTTCCAAACTGGAACAACACTCAACCTATCTCGGTCTATTCTTTTGATT  
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GCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCTAACTCCGCCCATCCCGCCCCCTAACT  
CCGCCAGTTCCGCCCATTTCTCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCG  
CCTCTGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCT  
CCGGGAGCTTGATATATCCATTTTCGGATCTGATCAGCAGTGTTGACAATTAATCATCGGCATAGTATA  
TCGGCATAGTATAATACGACAAGGTGAGGAATGAAACCATGGCCAAGCCTTTGTCTCAAGAAGAATCCAC  
CCTCATTGAAAGAGCAACGGCTACAATCAACAGCATCCCCATCTCTGAAGACTACAGCGTCGCCAGCGCA  
GCTCTCTTAGCGACGGCCGCATCTTCACTGGTGTCATGTATATCATTTTTACTGGGGGACCTTGTGCAG  
AACTCGTGGTGCTGGGCACTGCTGCTGCTGCGGCAGCTGGCAACCTGACTTGTATCGTCGCGATCGGAAA  
TGAGAACAGGGGCATCTTGAGCCCTGCGGACGCTGCCGACAGGTGCTTCTCGATCTGCATCCTGGGATC  
AAAGCCATAGTGAAGGACAGTGATGGACAGCCGACGGCAGTTGGGATTCTGTGAATTGCTGCCCTCTGGTT  
ATGTGTGGGAGGGCTAAGCACTTCGTGGCCGAGGAGCAGGACTGACACGTGCTACGAGATTTTCGATTCCA  
CCGCCGCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGCTGGATGATCTCCAGCG  
CGGGGATCTCATGCTGGAGTTCTTCGCCACCCCACTTGTTTATTGCAGCTTATAATGGTTACAAATAA  
AGCAATAGCATCACAATTTACAAATAAAGCATTTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAAC  
TCATCAATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATA  
GCTGTTTCTGTGTGAAATTGTTATCCGCTCACAATCCACACAACATACGAGCCGGAAGCATAAAGTGT  
AAAGCCTGGGGTGCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGT  
CGGGAACCTGTGCTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTTGCGTATTGG  
GCGCTCTCCGCTCCTCGCTCACTGACTCGCTGCGCTCGGTGCTTCCGCTGCGCGAGCGGTATCAGCT  
CACTCAAAGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAG

Fig. 11 A

GCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGA  
CGAGCATCACAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCG  
TTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCT  
TTCTCCCTTCGGGAAGCGTGGCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGT  
TCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACCTAT  
CGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA  
GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGAC  
AGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGC  
AAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTGTTGCAAGCAGCAGATTACGCGCAGAAAAAAGGAT  
CTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAACTCACGTTAAGGGAT  
TTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCA  
ATCTAAAGTATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAG  
CGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG  
CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCA  
ATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTA  
TTAATTGTTGCCGGAAGCTAGAGTAAGTAGTTCCGCCAGTTAATAGTTTTCGCAACGTTGTTGCCATTGC  
TACAGGCATCGTGGTGTACGCTCGTTCGTTGGTATGGCTTCATTAGCTCCGGTTCQCAACGATCAAGG  
CGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTGAGAA  
GTAAGTTGGCCGAGTGTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATC  
CGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCG  
AGTTGCTCTTGCCCGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCA  
TTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACC  
CACTCGTGCACCCAACCTGATCTTCAGCATCTTTTACTTTTACCAGCGTTTCTGGGTGAGCAAAAACAGGA  
AGGCAAAATGCCGCAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTTC  
AATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAA  
TAAACAAATAGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

Fig. II B



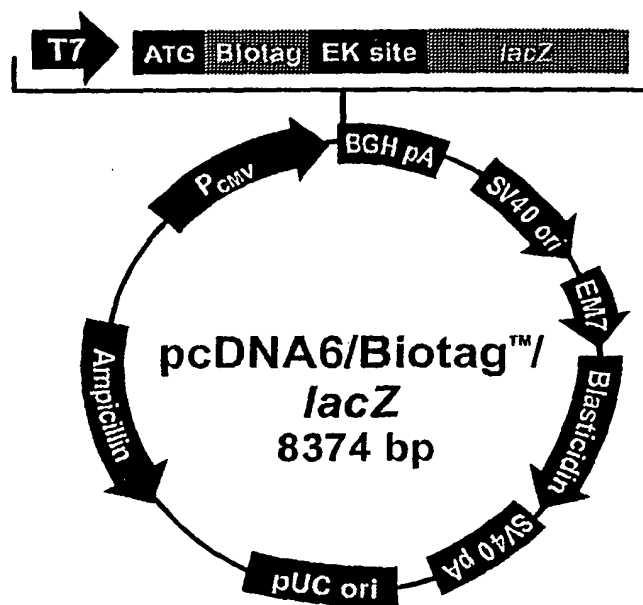


Fig. 12

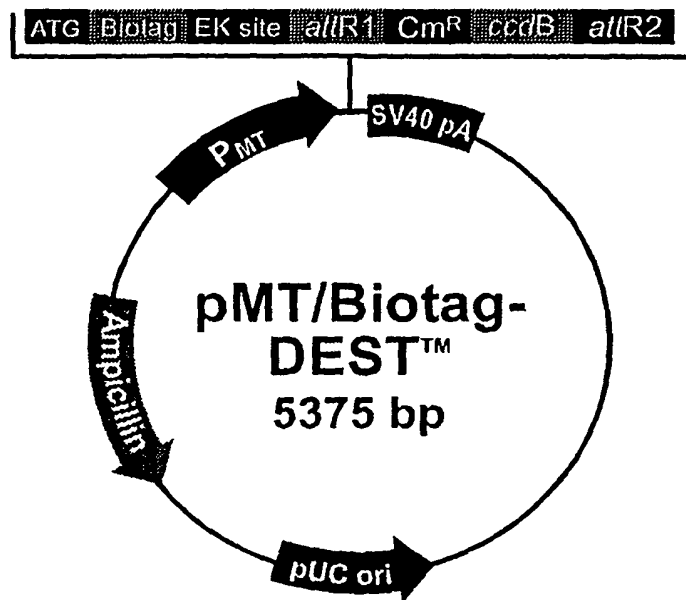


Fig.13

TCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCT  
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CTTAACCTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGCGGTGTGAAATACCGCACAGAT  
GCGTAAGGAGAAAAATACCGCATCAGGCGCCATTTCGCCATTTCAGGCTGCGCAACTGTTGGGAAGGGCGATC  
GGTGCGGGCCTCTTCGCTATTACGCCAGCTGGCGAAAGGGGGATGTGCTGCAAGGCGATTAAGTTGGGTA  
ACGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGCCAGTGAATTAATTCGTTGCAGGA  
CAGGATGTGGTGCCCGATGTGACTAGCTCTTTGCTGCAGGCCGTCCTATCCTCTGGTTCCGATAAGAGAC  
CCAGAACCTCCGGCCCCCACC GCCCACC GCCCACC CCATACATATGTGGTACGCAAGTAAGAGTGCCTGC  
GCATGCCCCATGTGCCCCACCAAGAGTTTTGCATCCCATACAAGTCCCCAAAGTGGAGAACCGAACCAAT  
TCTTCGCGGGCAGAACAAAAGCTTCTGCACACGTCTCCACTCGAATTTGGAGCCGGCCGGCGTGTGCAAA  
AGAGGTGAATCGAACGAAAGACCCGTGTGTAAAGCCGCGTTTCCAAAATGTATAAAACCGAGAGCATCTG  
GCCAATGTGCATCAGTTGTGGTCAGCAGCAAAATCAAGTGAATCATCTCAGTGCAACTAAAGGGGGGATC  
TAGCGTTTTAACTTAAGCTTACCATGGGCGCCGGCACC CGGTGACCGCCCCGCTGGCGGGCACTATCTG  
GAAGGTGCTGGCCAGCGAAGGCCAGACGGTGGCCGCAGGCGAGGTGCTGCTGATTCTGGAAGCCATGAAG  
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TGGCGGTTCGGCGACACCCCTGATGACCCTGGCGGGCTCTGGATCCGATCTGTACGACGATGACGATAAGGT  
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ATTAGGCACCCAGGCTTTACACTTTATGCTTCCGGCTCGTATAATGTGTGGATTTTGAGTTAGGATCCG  
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CACATTCTTGCCCGCTGATGAATGCTCATCCGGAATTCGATATGGCAATGAAAGACGGTGAGCTGGTGA  
TATGGGATAGTGTTCACCTTGTACACCGTTTTCCATGAGCAAACTGAAACGTTTTTCATCGCTCTGGAG  
TGAATACCACGACGATTTCCGGCAGTTTCTACACATATATTGCAAGATGTGGCGTGTACGGTGAAAAAC  
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CCAGTTTTTGATTTAAACGTGGCCAATATGGACAACCTTCTTCGCCCCGTTTTTCACCATGGGCAATATTA  
TACGCAAGGCGACAAGGTGCTGATGCCGCTGGCGATTTCAGGTTTCATCATGCCGTCTGTGATGGCTCCAT  
GTCGGCAGAATGCTTAATGAATTACAACAGTACTGCGATGAGTGGCAGGGCGGGCGTAAACGCGTGAT  
CCGGCTTACTAAAAGCCAGATAACAGTATGCGTATTTGCGCGCTCGCGAACC GGTTGATACCCGAAGTAT  
GTCAAAAAGAGGTGTGCTATGAAGCAGCGTATTACAGTGACAGTTGACAGCGACAGCTATCAGTTGCTCA  
AGGCATATATGATGTCAATATCTCCGGTCTGGTAAGCACAACCATGCAGAATGAAGCCCGTCGTCTGCGT  
GCCGAACGCTGGAAAGCGGAAAATCAGGAAGGGATGGCTGAGGTGCGCCGGTTTTATTGAAATGAACGGCT  
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ATCGTCTGTTTGTGGATGTACAGAGTGATATTATTGACACGCCCGGGCGACGGATGGTGATCCCCCTGGC  
CAGTGACGCTCTGCTGTCAGATAAAGTCTCCCGTGAACTTTACCCGGTGGTGCATATCGGGGATGAAAGC  
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CATAAAGTGTAAGCCTGGGGTGCCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCC  
GCTTTCCAGTCGGGAAACCTGTGCTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT  
TGCGTATTGGGCGCTCTTCCGCTTCTCGCTCACTGACTCGCTGCGCTCGGTCTGCTGCGCTGCGGCGAGC  
GGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATG

Fig. 14A

TGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCC  
GCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAG  
ATACCAGGCGTTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATAC  
CTGTCCGCGTTTTCTCCCTTCGGGAAGCGTGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGG  
TGTAGGTCGTTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTACGCCCCGACCGCTGCGCCTTATC  
CGGTAACCTATCGTCTTGAGTCCAACCCGGAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAAC  
AGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACA  
CTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTC  
TTGATCCGGCAACAAACCACCGCTGGTAGCGGTGGTTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGA  
AAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAACGAAAACTCAC  
GTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTACCTAGATCCTTTTAAATTAAAAATGAAG  
TTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCCTTAATCAGTGAGGCA  
CCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGA  
TACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACC GGCTCCAGA  
TTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCC  
ATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTTCGCCAGTTAATAGTTTGCGCAACGTTG  
TTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCGTTTTGGTATGGCTTCATTCAGCTCCGGTTCCTCA  
ACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAGCGTTAGCTCCTTCGGTCCTCCGATC  
GTTGTCAGAAAGTAAGTTGGCCGAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTG  
TCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGAT  
GCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAA  
GTGCTCATCATTGGAACCGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTT  
CGATGTAACCCACTCGTGACCCCACTGATCTTCAGCATCTTTTACTTTACCAGCGTTTCTGGGTGAGC  
AAAAACAGGAAGGCAAAATGCCGCAAAAAGGGAATAAGGGCGACACGGAATGTTGAATACTCATACTC  
TTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTA  
TTTAGAAAAATAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGCTAAGAAAC  
CATTATTATCATGACATTAACCTATAAAAAATAGGCGTATCACGAGGCCCTTTCGT

Fig. 14B

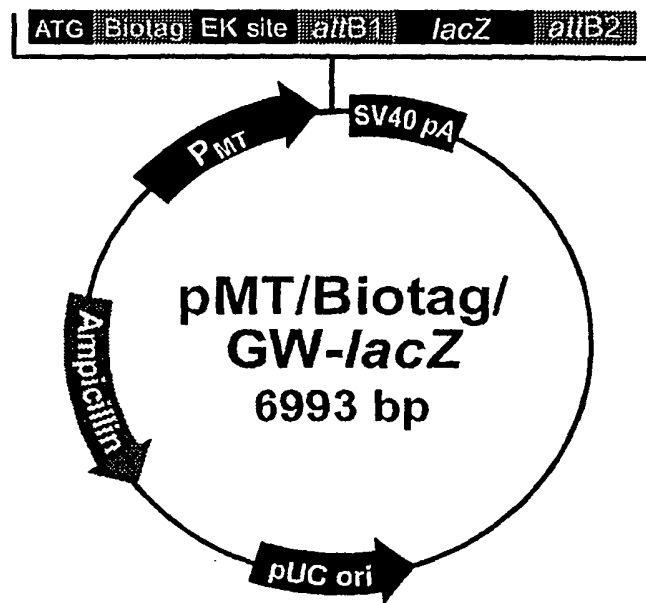


Fig. 15

- Shaded regions correspond to those DNA sequences transferred from the entry clone into the pET104-DEST™ vector by recombination. Non-shaded regions are derived from the pET104-DEST™ vector.
- Bases 568 and 2230 of the pET104-DEST™ sequence are marked.
- The biotin binding site is labeled with a \*.

121 ATAGGCGCCA GCAACCGCAC CTGTGGCGCC GGTGATGCCG GCCACGATGC GTCCGGCGTA GAGGATCGAG ATCTCGATCC

T7 promoter/priming site

T7 promoter      lac operator

201 CGCGAAATTA ATACGACTCA CTATAGGGGA ATTGTGAGCG GATAACAATT CCCCTCTAGA AATAATTTTG TTTAACTTTA

Biotag™

281 AGAAGGAGAT ATACAT **Met** Gly Ala Gly Thr Pro Val Thr Ala Pro Leu Ala Gly Thr Ile Trp Lys Val

RBS

351 Leu Ala Ser Glu Gly Gln Thr Val Ala Ala Gly Glu Val Leu Leu Ile Leu Glu Ala Met Lys Met

Biotin binding site

417 Glu Thr Glu Ile Arg Ala Ala Gln Ala Gly Thr Val Arg Gly Ile Ala Val Lys Ala Gly Asp Ala

Biotag™ forward priming site

483 Val Ala Val Gly Asp Thr Leu Met Thr Leu Ala Gly Ser Gly Ser Asp Leu Tyr Asp Asp Asp Asp

EY recognition site

549 Lys Gly Ile Ile Thr Ser Leu Tyr Lys Lys Ala Gly ... \*\*\*

568      2230

549 AAG GGA ATT ATC ACA AGT TTT **GENE** C TTGTACAAAG

EY cleavage site      attB1      attB2      T7 reverse priming site

2241 TGGTGATAAT TAATTAAGAT AGCTCAGATC CGGCTGCTAA CAAAGCCCGA AAGGAAGCTG AGTTGGCTGC TGCCACCGCT

2321 GAGCAATAAC TAGCATAACC

Fig. 16

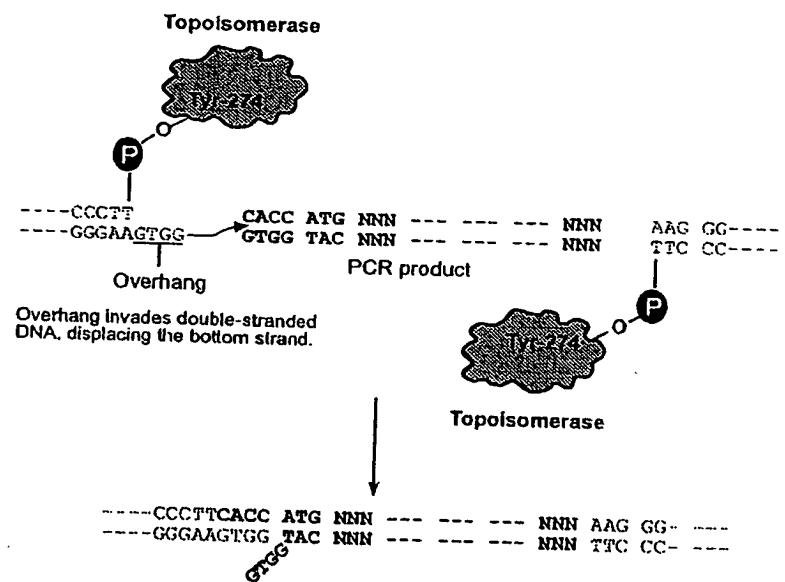
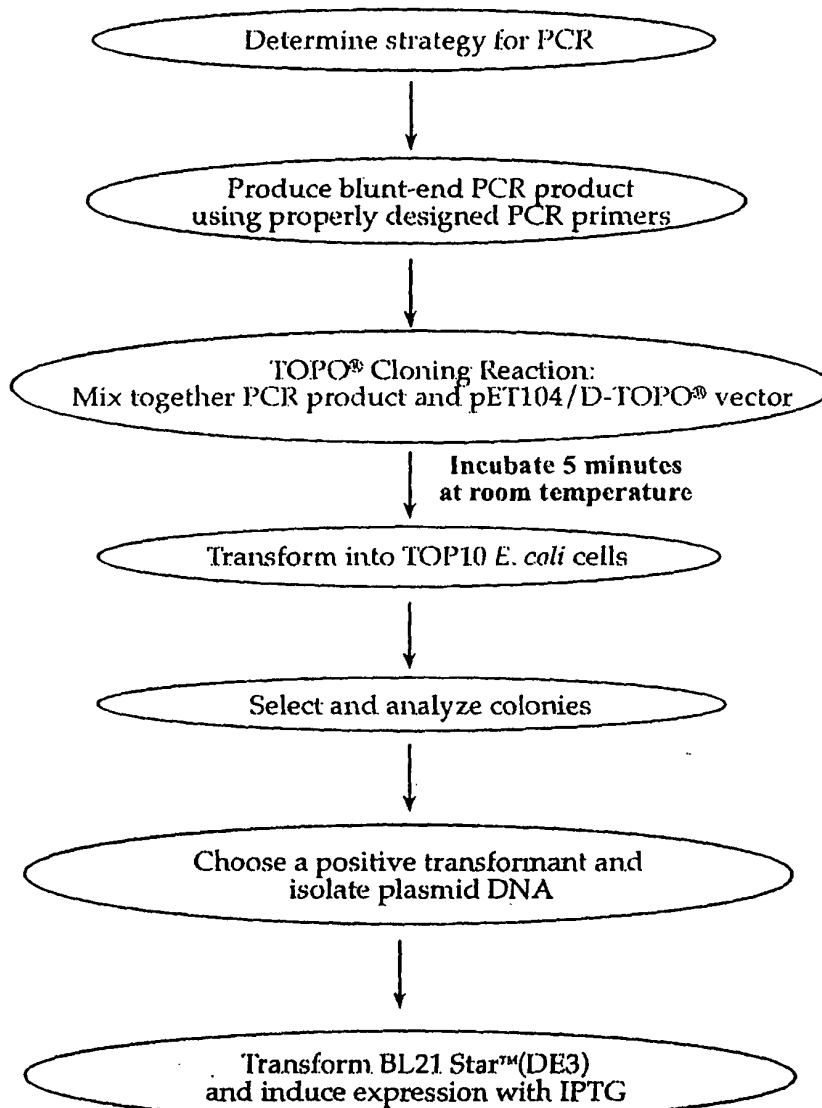


Fig.17

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### Flow Chart

The flow chart below describes the general steps required to clone and express your blunt-end PCR product.



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Fig. 18





- Shaded regions correspond to those DNA sequences transferred from the entry clone into the pcDNA6/Biotag-DEST™ vector by recombination. Non-shaded regions are derived from the pcDNA6/Biotag-DEST™ vector.
- Bases 1191 and 2853 of the pcDNA6/Biotag-DEST™ sequence are marked.
- The biotin binding site is labeled with a \*.
- Potential stop codons are underlined.

761 CCCATTGACG <sup>CAAT</sup> CAAATGGGCG GTAGGCGTGT ACGGTGGGAG <sup>TATA</sup> GTCTATATAA GCAGAGCTCT CTGGCTAACT AGAGAACCCA <sup>3' end of CMV promoter</sup> <sup>Putative transcriptional start</sup>

841 CTGCTTACTG GCTTATCGAA <sup>T7 promoter/priming site</sup> ATTAATACGA CTCACTATAG GGAGACCCAA GCTGGCTAGC GTTTAACTT AAGCTTACC **ATG** **Met**

<sup>Biotag™</sup>

923 Gly Ala Gly Thr Pro Val Thr Ala Pro Leu Ala Gly Thr Ile Trp Lys Val Leu Ala Ser Glu Gly  
GGC GCC GGC ACC CCG GTG ACC GCC CCG CTG GCG GGC ACT ATC TGG AAG GTG CTG GCC AGC GAA GGC

989 Gln Thr Val Ala Ala Gly Glu Val Leu Leu Ile Leu Glu Ala Met Lys Met Glu Thr Glu Ile Arg  
CAG ACG GTG GCC GCA GGC GAG GTG CTG CTG ATT CTG GAA GCC ATG AAG ATG GAA ACC GAA ATC CGC

<sup>Biotin binding site</sup>

1055 Ala Ala Gln Ala Gly Thr Val Arg Gly Ile Ala Val Lys Ala Gly Asp Ala Val Ala Val Gly Asp  
GCC GCG CAG GCC GGG ACC GTG CCG GGT ATC GCG GTG AAA GCC GGC GAC GCG GTG GCG GTC GGC GAC

<sup>Biotag™ forward priming site</sup> <sup>EK recognition site</sup> <sup>EK cleavage site</sup>

1121 Thr Leu Met Thr Leu Ala Gly Ser Gly Ser Asp Leu Tyr Asp Asp Asp Asp Lys Val His Gln Thr  
ACC CTG ATG ACC CTG GCG GGC TCT GGA TCC GAT CTG TAC GAC GAT GAC GAT AAG GTC CAT CAA ACA  
CAT GTA GTT **TGT**

1191 2853

1187 Ser Leu Tyr Lys Lys Ala Gly ... ... \*\*\* CTTGTACA AAGTGGTGT AATTATTAA  
AGT TT TTT  
TCA AAC ATG TTT

<sup>attB1</sup> <sup>BGH reverse priming site</sup> <sup>attB2</sup>

2881 GATCTAGAGG GCCCGTTTAA ACCCGCTGAT CAGCCTCGAC TGTGCCTTCT AGTTGCCAGC CATCTGTTGT

Fig. 20

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### Flow Chart

The flow chart below outlines the experimental steps necessary to clone and express your blunt-end PCR product.

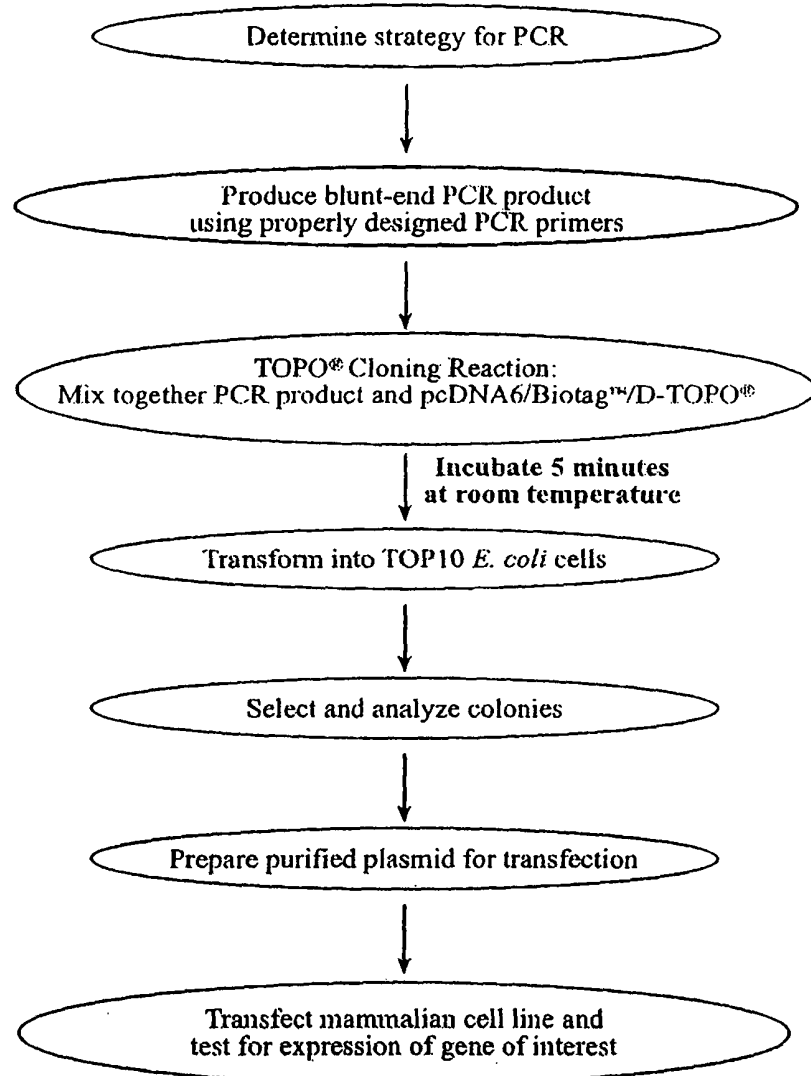


Fig. 21

761 CCCATTGACG <sup>CAAT</sup> CAAATGGGCG GTAGGCGTGT ACGGTGGGAG <sup>TATA</sup> GTCTATATAA GCAGAGCTCT <sup>3' end of CMV promoter</sup> CTGGCTAACT <sup>Putative transcriptional start</sup> AGAGAACCCA  
 841 CTGCTTACTG GCTTATCGAA <sup>T7 promoter/priming site</sup> ATTAATACGA CTCACTATAG GGAGACCCAA GCTGGCTAGC GTTTAAACTT AAGCTTACC **ATG**  
 923 <sup>Biotag™</sup> GGC GCC GGC ACC CCG GTG ACC GCC CCG CTG GCG GGC ACT ATC TGG AAG GTG CTG GCC AGC GAA GGC  
 Gly Ala Gly Thr Pro Val Thr Ala Pro Leu Ala Gly Thr Ile Trp Lys Val Leu Ala Ser Glu Gly  
 989 CAG ACG GTG GCC GCA GGC GAG GTG CTG CTG ATT CTG GAA GCC ATG AAG ATG GAA ACC GAA ATC CCG  
 Gln Thr Val Ala Ala Gly Glu Val Leu Leu Ile Leu Glu Ala Met Lys Met Glu Thr Glu Ile Arg  
<sup>Biotin binding site</sup>  
 1055 GCC GCG CAG GCC GGG ACC GTG CCG GGT ATC GCG GTG AAA SCC GGC GAC GCG GTG CCG GTC GGC GAC  
 Ala Ala Gln Ala Gly Thr Val Arg Gly Ile Ala Val Lys Ala Gly Asp Ala Val Ala Val Gly Asp  
<sup>Biotag™ forward priming site</sup>  
 1121 ACC CTG ATG ACC CTG GCG GGC TCT GGA TCC GAT CTG TAC GAC GAT GAC GAT AAG GTA CCT AGG ATC  
 Thr Leu Met Thr Leu Ala Gly Ser Gly Ser Asp Leu Tyr <sup>Asp718</sup> Asp <sup>Kpn I</sup> Asp Asp Asp Lys Val Pro Arg Ile  
<sup>EK recognition site</sup> <sup>Xba I</sup> <sup>Asp I</sup> <sup>EK cleavage site</sup>  
 1187 CAG TGT GGT GGA ATT GAT CCC TT ACC AAGGGCG TCGAGTCTAG AGGGCCCGTT TAAACCCGCT  
 Gln Cys Gly Gly Ile Asp Pro Phe Thr  
<sup>BGH reverse priming site</sup>  
 1251 GATCAGCCTC GACTGTGCC TCTAGTTGCC AGCCATCTGT TGTTCGCCCC

Fig. 22

- Shaded regions correspond to those DNA sequences transferred from the entry clone into the pMT/Biotag™-DEST vector by recombination. Non-shaded regions are derived from the pMT/Biotag™-DEST vector.
- Bases 1135 and 2797 of the pMT/Biotag™-DEST sequence are marked.
- The biotin binding site is labeled with a \*.
- Potential stop codons are underlined.

5' end of metallothionein promoter Metal regulatory region

411 CGTTGCAGGA CAGGATGTGG TGCCCGATGT GACTAGCTCT TTGCTGCAGG CCGTCCTATC CTCTGGTTCC GATAAGAGAC CCAGAACTCC

501 GGCCCCCACC CCCCCACGC CCCCCCATA CATATGTGGT ACGCAAGTAA GAGTGCCTGC GCATGCCCA TGTGCCCCAC CAAGAGTTT

591 GCATCCGATA CAAGTCCCCA AAGTGGAGAA CCGAACCAAT TCTTCGCGGG CAGAACAAAA GCTTCTGCAC ACGTCTCCAC TCGAATTGCG

681 AGCCGGCCCG CGTGTGCHAA AGAGGTGAAT CGAACGAAG ACCCGTGTGT AAAGCCCGGT TTCCAAATG TATAAACCG AGAGCATCTG

771 GCCAATGTGC ATCAGTTGTG GTCAGCAGCA AAATCAAGTG AATCATCTCA GTGCAACTAA AGGGGGGATC TAGCGTTTAA ACTTAAGCTT

861 ACC ATG GGC GCC GGC ACC CCG GTG ACC GCC CCG CTG GCG GGC ACT ATC TGG AAG GTG CTG GCC AGC GAA

930 GGC CAG ACC GTG GCC GCA GGC GAG GTG CTG CTG ATT CTG GAA GCC ATG AAG ATG GAA ACC GAA ATC CGC

999 Ala Ala Gln Ala Gly Thr Val Arg Gly Ile Ala Val Lys Ala Gly Asp Ala Val Ala Val Gly Asp Thr  
GCC GCG CAG GCC GGG ACC GTG CCG GGT ATC GCG GTG AAA GCC GGC GAC GCG GTG GCG GTC GGC GAC ACC

1068 Leu Met Thr Leu Ala Gly Ser Gly Ser Asp Leu Tyr Asp Asp Asp Asp Lys Val His Gln Thr Ser Leu  
CTG ATG ACC CTG GCG GGC TCT GGA TCC GAT CTG TAC GAC GAT GAC GAT AAG GTA CAT CAA ACA AGT TTT  
CAT GTA GTT TGT TCA AAC

1137 Tyr Lys Lys Ala Gly ... \*\*\*  
ATG TTT TTT GGT GCG AND GENE NACCC AGGCTT CTGG TACAAAGTGG TGATAATTAA TTAAGATCTA GAGGGCCCGT

attB1 attB2

continued on next page

Fig. 23

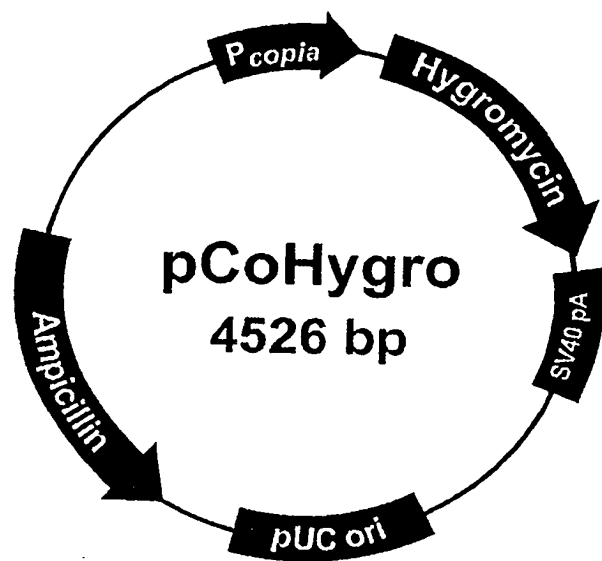


Fig. 24

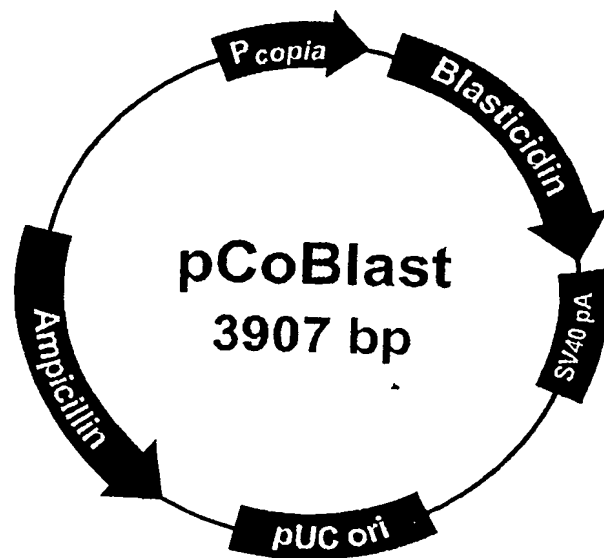


Fig. 25